3. METHODS USED OR PROPOSED BY OTHER AGENCIES

3.1. ACGIH

ACGIH first discussed its procedure for dealing with exposure to mixtures in 1963 (ACGIH 1984); the procedure has changed but little to the present day. ACGIH (2000) recommends additivity approaches for the assessment of occupational hazard. For mixtures of two or more hazardous substances that act on the same organ system, the ratio of the exposure concentration to the threshold limit value (TLV) for each component is summed (dose addition, hazard index approach). If the sum exceeds one, then the TLV for the mixture is considered as being exceeded. Exceptions to the hazard index approach can be made when there is good reason to expect that the chief effects of the components are independent. According to ACGIH, an example would be when the components produce purely local effects on different organ systems. When the effects are expected to be independent, the TLV for the mixture is exceeded only if at least one component has a hazard quotient that exceeds unity. In effect, the hazard index for the mixture would be the highest hazard quotient for any of the components. (This resembles response addition with completely positive correlation of tolerances, Appendix A.) ACGIH recommends evaluating synergism or potentiation on a case by case basis, and further states that such interactions are characteristically exhibited at high concentrations and are less likely at low.

In the case when a process emits a number of harmful dusts, fumes, vapors, or gases, ACGIH states that frequently it may be feasible only to measure a single substance in order to evaluate the hazard. In this circumstance, the threshold limit for this substance should be reduced by a suitable factor, the magnitude of which takes into account the number, toxicity, and relative amounts of the other components typically present. This appears to be a combination indicator chemical/uncertainty factor approach. Some examples cited by ACGIH were welding, painting, and certain foundry operations.

3.2. OSHA

The Occupational Safety and Health Administration (OSHA 1993, 2001) also recommends a hazard index approach that employs the ratio of the exposure concentration to the PEL for each chemical and sums the ratios. If the sum of the ratios exceeds one, then the exposure limit for the mixture is exceeded. OSHA does not restrict the approach to chemicals with similar effects.

3.3. NIOSH

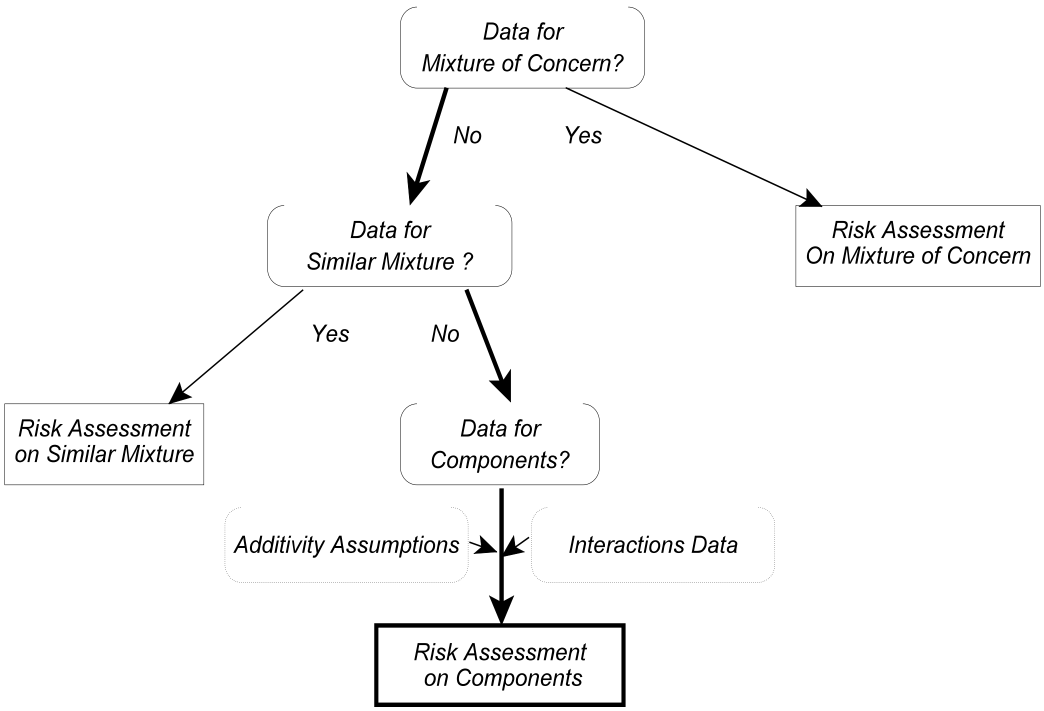
The National Institute for Occupational Safety and Health (NIOSH 1976) adopted a similar approach in recommending exposure limits for methylene chloride when carbon monoxide was also present because of the known additivity of the two chemicals with regard to formation of carboxyhemoglobin. NIOSH recommended that the sum of the ratios of each chemical to their recommended exposure limits not exceed one, and that the permissible exposure limits for methylene chloride be adjusted downward when carbon monoxide levels were greater than 9 ppm in order to keep the sum from exceeding unity. (More recent NIOSH [1992] recommendations are based on carcinogenicity.)

3.4. EPA

An overview of the EPA (1986) mixtures guidelines for risk assessment of chemical mixtures is provided in Figure 1. The guidelines recommend the use of exposure and health effects data for the mixture of concern or a similar mixture if available. If not, the use of data for the components is recommended. The components procedure is most commonly used, as indicated on the figure by the heavier arrows and box. When more than one of these approaches is feasible, EPA (1986) recommends a comparison of results from the different approaches.

The guidelines recommend the assessment of interactions data, when available, in terms of relevance to subchronic or chronic exposure and suitability for quantitatively altering the risk assessment. Interactions data are considered likely to be available mainly for pairs of chemicals, which could be assessed separately from those with no such information. The guidelines recommend, however, exploring the possibility that other components of the mixture may interfere with the interaction of the chemical pair on which quantitative interaction data are available. If interference appears likely, then quantitative alteration of the risk assessment may not be justifiable.

Figure 1. Overview of EPA Guidelines for Mixtures Risk Assessment



The assessment of the noncarcinogenic effects of the components usually proceeds by the hazard index method. Because it assumes dose additivity, the hazard index method is most suitable for chemicals with similar effects. If the mixture includes chemicals that have different effects, then EPA recommends the calculation of separate hazard indexes for each endpoint of concern. The guidelines mention that if data are sufficient to derive individual acceptable levels for a spectrum of effects, "the hazard index may suggest what types of effects might be expected from the mixture exposure." Subsequent guidance for Superfund risk assessment gave further explicit directions for the hazard index approach, including the combining of hazard indexes for multi-route exposure and the calculation of separate hazard indexes for different target organ toxicities (EPA 1989a). For carcinogenic effects, the guidelines recommend summing the risks across components, as discussed in Section 2.3.5. EPA (1999) is developing additional mixtures guidance for risk assessment, which will supplement the original EPA (1986) guidelines.

3.5. NAS/NRC

In 1972, at the request of the EPA, the NAS recommended health-based stream criteria for a large number of pollutants. A component of this appraisal was multiple chemical exposure (NAS 1974). The NAS recommended a hazard index approach, whereby the sum of the ratios of the measured concentrations to the acceptable concentrations for the components was to be kept at a level equal to or lower than unity.

In 1989, at the request of EPA, The Safe Drinking Water Committee of the National Research Council (NRC 1989) suggested possible modifications of the then current approaches for estimating the toxicity of mixtures in drinking water. The NRC suggested that mixture components be grouped by endpoint, such as specific organ toxicity and carcinogenicity in order to assess their combined risk or hazard.

For noncancer endpoints, the NRC suggested a modified hazard index that sums similar toxicities and an uncertainty factor for possible synergism, depending on the information regarding interactions and the concentrations of the components. The uncertainty factor could range from 1 to 100. If information regarding potential interactions is available and suggests interactions are not likely, or if the concentrations are low, the uncertainty factor could be set at 1. The NRC also suggested that separate hazard indexes be calculated for each toxic endpoint, including those that occur at higher exposure levels than the endpoint that is the basis for the acceptable exposure level for a component. A weighting factor would be applied to account for the lesser sensitivity of the other endpoints, unless an acceptable exposure level for the other endpoints was available. The method is similar to the TTD modification of the hazard index method, discussed previously, except the NRC further suggested summing the hazard indexes across all toxic endpoints.

For carcinogenic endpoints, the NRC concluded that it was appropriate to sum the risks (response addition with completely negative correlation of tolerances) for low-dose exposure to a mixture of carcinogens (doses with relative risks of less than 1.01).